FORM PTO-14	449	US Dept. of C	Commerce	ATTORNEY DOCKET NO.		SERIAL NO).	
		Patent and Tr. Office	ademark	4012-113 DIV2		09/430,735		
tadi 13	CME	Office NTAL INFORM	ATION	APPLICANT		09/430,733		
		URE STATEM		7 T LIOMIN			•	
				Ekwuribe et al.			· 	
(use several sheets if necessary)		FILING DATE GROUP						
				October 29, 1999		+018 11	,39	ļ
			U.S.	PATENT DOCUMENTS				
EXAMINER		PATENT	-				FILING IF APPRO	
INITIAL		NUMBER	ISSUE DATE	NAME	CLASS	SUBCLASS	IF APPRO	PRIATE
1								
				010				
	+			1/44	-			
				JAN 27 2000 50				
				ADEMARKOR				
<u> </u>				Trium.				
	Ì							
				GN PATENT DOCUMENTS			mp . NO.	
		DOCUMENT	PUBLICATION	COUNTRY	CLASS	SUBCLASS	TRANSI YES	LATION NO
		NUMBER	DATE	COUNTRY	CLASS	SUBCLASS		
						<u> </u>	·	
		OTHER DOCU	MENTS (Inclu	ding Author, Title, Journal-Da	ate, Page N	lumber, Etc.)		
1/1	AA	Delgado et al. '	"The Uses and Pr	roperties of PEG-Linked Protein	is". Critica	l Review in Th	erapeutic i	Drug
	-	Carrier System	s, 9(3, 4):249-30	14 (1992).	•			
				·		·		
							;	
					*	*****		
	•							
,								
				Continue on Page				
EXAMINER					DATE C	ONSIDERED		
		B. cus	P			-bilo3		
EVANDED	T i.e.i	Viscinal and	vidared subather	or not citation is in conformance	with MPF	P 8 609. Drav	v line throu	igh .
citation if not	in con	ii ii citation cons iformance and n	ot considered. In	or not chation is in comormance iclude copy of this form with nex	xt commun	ication to the	applicant.	

1

	اتم	· • · · · · · · · · · · · · · · · · · ·				077111 110
FORM PTO-14	49	US Dept. of Commerce	ATTORN	EY DOCKET	NO.	SERIAL NO.
		Patent and Trademark Office	,,,,	DIV.		09/430,735
			4012-113		TA	
		CLOSURE STATEMENT	APPLICA		'~%	
INFORMATIO	אום אינ	CLOSURE STATEMENT	Ekwuribe	et al.	1.	
(1120	~~~~	Laborta if necessary)	FILING D	ATE	700m C)	GROUP
(use	severa	l sheets if necessary)		29, 1999	13 gs	
			00.000.	, (4's	48	1639
		-		DEN	AHKO	
	0	THER DOCUMENTS (Includ	ing Author	, Title, Journ	al-Date, Pag	e Number, Etc.)
Dal C	CM	Pardridge, W.M., "Blood-Brain	Barrier Per	tide Transpor	t and Peptide	Drug Delivery to the Brain," Amer.
	8	Chem Soc. 1995: 265-296.				
\ \ (CN	Pardridge, W.M., "CNS Drug D	esign Base	d on Principle:	s of Blood-Br	ain Barrier Transport," J.
	89	Neurochem., 1998, 70 (5): 178	1-1792.			
	CO 6	Pardridge, W.M., "New Approa	iches to Dru	g Delivery Th	rough the Blo	ood-Brain Barrier," Trends in
		Biotechnology, 1994: 239-245.				L. A. J. L. Between stable lie
	CP a			elivery of a Le	eucine-Enkepi	halin Analogue by Retrometabolic
	(6)	Design," J. Med. Chem 39 (24)		Allaman	Dagulting fro	m High Molocular Weight Insulin
((CQ 6				Resulting iro	m High-Molecular Weight Insulin
<u> </u>	<u> </u>	Aggregates," Diabetes, 1990, 39	91. 128-133.	nt Aggregates	of Inculin in	Blood of Insulin-Using Diabetic
11	CR 🛭	Patients," Diabetes, 1987, 36: 8	es to Covan	an Aggregates	s or msum m	Blood of Histinii-Osing Diabetic
E A	CC m		roach to the	Oral Adminis	tration of Insi	ulin and Other Pentide Drugs."
	CS 8	Science, 1986, 233: 1081-1084		Olai Adillillis	tration or mist	ann and caler replies 21-55,
100	CT a	Sakaeda T et al "Conjugatio	n with L-Gl	utamic Acid fo	or Brain Drug	Delivery," Proceed. Intern. Symp.
`	C1 W	Control. Rel. Bioact. Mater., 19	66, 23: 607	-608.		
1 1	CU 6	Shashoua V.E., et al., "γ-Amino	butyric Aci	d Esters. 1. S	ynthesis, Brai	n Uptake, and Pharmacological
		Studies of Aliphatic and Steroic	l Esters of y	-Aminobutyric	c Acid," J. Me	ed. Chem., 1984, 27 (5): 660-664.
	CV v	Shashoua, V.E., et al., "N-Doco	sahexaenoy	l, 3 Hydroxyt	yramine: A D	opaminergic Compound that
	e l	Penetrates the Blood-Brain Bar	rier and Sup	presses Appe	tite," Life Sci	ences, 58 (16): 1347-1354.
	CW	Sim, L., et al., "In vitro Autorac	diography o	f Receptor-Ac	tivated G Pro	teins in Rat Brain by Agonist-
	•		nio]-Tripho:	phate Binding	g," Proc. Natl.	. Acad. Sci., USA, 1995, 92: 7242-
		7246.				0 1005 007 316
	CX 😼	Terasaki, T., et al., "Oligopepti				
	CY	Tsuzuki, N., et al., "Rabid Com	munication	Adamantane	as a Brain-D	irected Drug Carrier for Poorly
	0	Absorbed Drug: Antinociceptive	e Effects of	[D-Ala2] Leu	-Enkephalin I	Derivatives Conjugated with the 1-
		Adamantane Moiety." Biochem	nical Pharma	cology, 1991	, 41 (4): R5-R	.8.
	CZ	Wagner, J., et al., "Neuropharm	nacology of	Endogenous (Opioid Peptid	es," Psychopharmacology: The
			1995: 519-	529.		25172 1 1 1 1 7 7
	DA a	Weber, S.J., et al., "Distribution	n and Analg	esia of ['H][D	-PEN", D-PE	N' J Enkephalin and Two
		l Halogenated Analogs after Intr	avenous Ad	ministration,"	J. Pharm. Exp	per. Ther., 1991, 259: 1109-1112.
}.	DB	Weber, S.J., et al., "Whole Boo	ly and Brair	Distribution	of [H]Cyclic	[D-PEN ² , D-PEN ⁵] Enkephalin after
	•		rai and Subo	cutaneous Adn	innistration,"	J. Pharm. Exper. Ther., 1992, 263:
[[]		1308-1316.			***	
			-			<u> </u>
			Continue	on Page		
Examiner		· · · · · · · · · · · · · · · · · · ·		DATE CON	SIDERED	
LAMINICI	4	_			103	
	В	CRC5 A				
EXAMINER:	Initial	if citation considered, whether of	or not citatio	n is in confor	nance with M	IPEP § 609; Draw line through
citation if not i	in conf	ormance and not considered. In	clude copy	of this form wi	th next comm	nunication to the applicant.

FORM PTO-1449 US Dept. of Commerce Patent and Trademark Office		ATTORNEY DOCKET NO	SERIAL NO 09/430,73					
			4012-113 DIV2					
!				APPLICANT	RECE			
INFORMAT	ION DI	SCLOSURE ST	ATEMENT	Ekwuribe et al.	REC		ACL	
(u:	se sever	al sheets if nece	ssary)	FILING DATE	GROUP	1160 14	1999	
				October 29, 1999	1639	00/20		
			U.S.	PATENT DOCUMENTS			TECH CENTER 16	00/290
EXAMINER INITIAL		PATENT NUMBER	ISSUE DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE	
11	AA	4,585,754	29 Apr. 1986	Meisner et al.	514	8]
	AB	4,179,337	18 Dec. 1979	Davis et al.	435	181		
	AC	4,003,792	18 Jan. 1977	Mill et al.	195	63	-	
- ///	AD	4,849,405	18 Jul. 1989	Ecanow	TEL	3		1
111	AE	5,013,556	7 May 1991	Woodle et al.	- 1 MB-8			
MA	AF	4,963,367	16 Oct. 1990	Ecanow	424	785		1
	AG	4,044,196	23 Aug. 1977	Hüper et al.	THADEN	271		
m	AH	4,717,566	5 Jan. 1988	Eckenhoff et al.	424	438		1
M	ΑI	4,698,264	6 Oct. 1987	Steinke	428	40-2_2		
M	AJ	4,684,524	4 Aug. 1987	Eckenhoff et al.	424	469		
and	AK	4,410,547	18 Oct. 1983	Ueno et al.	424	317		
IM	AL	3,256,153	14 Jun. 1966	Heimlich	167	82		
M	AM	4,935,246	19 Jun. 1990	Ahrens	424	490		
(11)	AN	4,797,288	10 Jan 1989	Sharma et al.	424	47.6		
M	AO	4,744,976	17 May 1988	Snipes et al.	424	408		
M	AP	5,055,304	8 Oct. 1991	Makino et al.	424	465		
m	AQ	5,055,300	8 Oct. 1991	Gupta	424	409		
m	AR	4,772,471	20 Sep. 1988	Vanlerberghe et al.	424	450		
m	AS	5,093,198	3 Mar. 1992	Speaker et al.	428	402.21		
Ma	AT	4,840,799	20 Jun. 1989	Appelgren et al.	424	4.93		
1/h	AU	4,622,392	11 Nov. 1986	Hong et al.	536	29		
M	AV	5,653,987	5 Aug. 1997	Modi et al.	424	604		
11/2	AW	5,792,834	11 Aug. 1998	Hakimi et al.	530	351]
	AX	5,595,732	21 Jan. 1997	Hakimi et al.	424	85.7	7	_
	AY	5,539,063	23 Jul. 1996	Hakimi et al.	625	403		1
				Continue on page 2]
EXAMINER	В	ceisp				DATE CON		
EXAMINER	t: Initia	l if citation cons	idered, whether o	r not citation is in conforman	ce with MPEI	§ 609; Draw	line through	
citation if no	t in con	formance and no	ot considered. Inc	clude copy of this form with n	ext communic	cation to the ap	oplicant.	

FORM PTO-	RM PTO-1449 US Dept Patent ar			ATTORNEY DOCKET NO.		SERIAL NO 09/430,735		
		Patent and Tra	demark Office	4012-113 DIV2		U2143U,132	,	
				APPLICANT				
INFORMATI	ION DI	SCLOSURE STA	ATEMENT	Ekwuribe et al.				
(us	se sever	al sheets if neces	sary)	FILING DATE		GROUP		
				October 29, 1999	1	16	39	
EXAMINER INITIAL 7	1	PATENT NUMBER	ISSUE DATE	NAME	CLASS	SUBCLASS	FILING IF APPRO	
1/1	AZ	5,559,213	24 Sep 1996	Hakimi et al.	530	351)	
M	BA	5,747,646	5 May 1998	Hakimi et al.	530	351	-	<u> </u>
M	BB	5,286,637	15 Feb. 1994	Veronese et al.	PURG	183		-
M	BC	5,631,263	20 May 1997	Portoghese et al.	हित्र	27.9	l	
	BD	5,602,099	11 Feb. 1997	Schiller Etc -	7 1999 500	18	J	_
11/2	BE	5,545,719	13 Aug. 1996	Shashoua et al. Dooley et al.	5.36	345	_	_
	BF	5,641,861	24 Jun. 1997	Dooley et al.	IARKOT 30	329		_
11/12	BG	5,663,295	2 Sep. 1997	Moreau et al.	530	330	-	
ALC	ВН	5,786,447	28 Jul. 1998	Schiller et al.	531	307	7	
	BI	4,939,174	3 Jul. 1990	Shashoua	514	549		_
	BJ	5,932,462	Aug. 3, 1999	Harris et al.	435	188	-	
			FODEIC	ON PATENT DOCUMENTS				
	_			INTAILINI DOCUMENTS				
		DOCUMENT NUMBER	PUBLICATION DATE	COUNTRY	CLASS	SUBCLASS	TRANSL YES	ATION NO
			PUBLICATION	•	CLASS	SUBCLASS		
		NUMBER	PUBLICATION DATE	COUNTRY				NO
	(NUMBER OTHER DOCU	PUBLICATION DATE MENTS (Includ	COUNTRY ing Author, Title, Journal-Da	te, Page N	umber, Etc.)	YES	NO X
ea	BK t	NUMBER OTHER DOCU Alyautdin, R.N	PUBLICATION DATE MENTS (Includ	COUNTRY	te, Page N	umber, Etc.) with Polysorb	YES	NO X
M	BK	OTHER DOCU Alyautdin, R.N. Polybutylcyand Aoshima, M. e	PUBLICATION DATE MENTS (Includ I., "Delivery of L bacrylate Nanopa t al., "N ⁴ -Beheno	ing Author, Title, Journal-Da operamide Across the Blood-Bi rticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto	te, Page Norain Barrier 4: 325-328	umber, Etc.) with Polysorb	YES	NO X
M	BK t BL g	Alyautdin, R.N. Polybutylcyand Aoshima, M. e Cancer Researd Banting, R. G.,	MENTS (Includ I., "Delivery of L pacrylate Nanopa t al., "N ⁴ -Beheno ch, 1977, 37: 248 et al., "Pancreat	ing Author, Title, Journal-Da operamide Across the Blood-Bi rticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto	rain Barrier 4: 325-328 ssine as a Po	with Polysorb	ate 80-Coa	NO X ated
	BK &	Alyautdin, R.N. Polybutylcyand Aoshima, M. e Cancer Researd Banting, R. G., Assoc. J. 1922	MENTS (Includ I., "Delivery of L pacrylate Nanopa t al., "N ⁴ -Beheno ch, 1977, 37: 248 et al., "Pancreat t, 12: 141-146.	ing Author, Title, Journal-Da operamide Across the Blood-Br rticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto 1-2486. ic Extracts in the Treatment of I	rain Barrier 4: 325-328 sine as a Po	with Polysorb tential New A	ate 80-Coa	NO X ated agent,"
	BK t BL g	Alyautdin, R.N. Polybutylcyand Aoshima, M. e Cancer Researd Banting, R. G., Assoc. J. 1922 Baker, D. C. et	PUBLICATION DATE MENTS (Includ I., "Delivery of L bacrylate Nanopa t al., "N ⁴ -Beheno ch, 1977, 37: 248 et al., "Pancreat 12: 141-146. t al., "Prodrugs of	ing Author, Title, Journal-Da operamide Across the Blood-Br rticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto 1-2486.	rain Barrier 4: 325-328 sine as a Po	with Polysorb tential New A	ate 80-Coa	NO X ated agent,"
en	BK &	Alyautdin, R.N. Polybutylcyand Aoshima, M. e Cancer Researd Banting, R. G., Assoc. J. 1922 Baker, D. C. et (O-Acyl) Deriv Banks, W.A., e	PUBLICATION DATE MENTS (Includ I., "Delivery of L bacrylate Nanopa t al., "N ⁴ -Beheno ch, 1977, 37: 248 et al., "Pancreat t al., "Prodrugs of vatives," J. Med. et al., "Passage of	ing Author, Title, Journal-Da operamide Across the Blood-Br rticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto 1-2486. ic Extracts in the Treatment of I f 9-β-D-Arabinofuranosyladenin Chem., 1978, 21(12): 1218-12: Peptides Across the Blood-Bra	rain Barrier 4: 325-328 sine as a Po Diabetes Mo ne. 1. Synth 21.	with Polysorb tential New A ellitus," The C essis and Evalu	ate 80-Coantitumor A	NO X ated agent,"
	BK to BL p BM to BN to BO to	Alyautdin, R.N. Polybutylcyand Aoshima, M. e Cancer Researd Banting, R. G., Assoc. J. 1922 Baker, D. C. et (O-Acyl) Deriv Banks, W.A., e Perspectives,"	PUBLICATION DATE MENTS (Includ I., "Delivery of L bacrylate Nanopa t al., "N ⁴ -Beheno ch, 1977, 37: 248 tet al., "Pancreat tal., "Prodrugs of vatives," J. Med. et al., "Passage of Life Sciences, 19	ing Author, Title, Journal-Da operamide Across the Blood-Briticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto 1-2486. ic Extracts in the Treatment of late of Po-β-D-Arabinofuranosyladening Chem., 1978, 21(12): 1218-12. Peptides Across the Blood-Braine, 59 (23), 1923-1943.	te, Page Norain Barrier 4: 325-328 sine as a Po Diabetes Mone. 1. Synth 21. nin Barrier:	with Polysorb otential New A cellitus," The C esis and Evalu	ate 80-Coa antitumor A anadian M ation of So gical	NO X ated Agent," ed.
	BK & BL & BN	Alyautdin, R.N. Polybutylcyand Aoshima, M. e Cancer Researd Banting, R. G., Assoc. J. 1922. Baker, D. C. et (O-Acyl) Deriv Banks, W.A., e Perspectives," Boccu, E. et al Pharm. Res. Co	PUBLICATION DATE MENTS (Includ I., "Delivery of L bacrylate Nanopa t al., "N ⁴ -Beheno ch, 1977, 37: 248 t et al., "Pancreat t 12: 141-146. t al., "Prodrugs of vatives," J. Med. et al., "Passage of Life Sciences, 19 t, "Pharmocokine tomm., 1982, 14:	ing Author, Title, Journal-Date operamide Across the Blood-Braticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto 1-2486. ic Extracts in the Treatment of 1 f. 9-β-D-Arabinofuranosyladenia Chem., 1978, 21(12): 1218-12. Peptides Across the Blood-Bratic Properties of Polyethylene Coll-120.	rain Barrier 4: 325-328 sine as a Po Diabetes Me ne. 1. Synth 21. nin Barrier: Glycol Deriv	with Polysorb otential New A ellitus," The C esis and Evalu Pathophysiolo	ate 80-Coa antitumor A anadian M ation of So gical	NO X ated Agent," ed. ome 5'-
M	BK to BL p BM to BN to BO to	Alyautdin, R.N. Polybutylcyand Aoshima, M. e Cancer Researd Banting, R. G., Assoc. J. 1922 Baker, D. C. et (O-Acyl) Deriv Banks, W.A., e Perspectives," Boccu, E. et al Pharm. Res. Co. Bodor, N., et a	PUBLICATION DATE MENTS (Includ I., "Delivery of L bacrylate Nanopa t al., "N ⁴ -Beheno ch, 1977, 37: 248 t et al., "Pancreat t 12: 141-146. t al., "Prodrugs of vatives," J. Med. et al., "Passage of Life Sciences, 19 t, "Pharmocokine tomm., 1982, 14:	ing Author, Title, Journal-Da operamide Across the Blood-Br rticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto 1-2486. ic Extracts in the Treatment of I f 9-β-D-Arabinofuranosyladenin Chem., 1978, 21(12): 1218-12. Feptides Across the Blood-Bra 196, 59 (23), 1923-1943. rtic Properties of Polyethylene (11-120. r Delivering Peptides into the C	rain Barrier 4: 325-328 sine as a Po Diabetes Me ne. 1. Synth 21. nin Barrier: Glycol Deriv	with Polysorb otential New A ellitus," The C esis and Evalu Pathophysiolo	ate 80-Coa antitumor A anadian M ation of So gical	NO X ated Agent," ed. ome 5'-
M	BK & BL & BN	Alyautdin, R.N. Polybutylcyand Aoshima, M. e Cancer Researd Banting, R. G., Assoc. J. 1922 Baker, D. C. et (O-Acyl) Deriv Banks, W.A., e Perspectives," Boccu, E. et al Pharm. Res. Co. Bodor, N., et a	PUBLICATION DATE MENTS (Includ I., "Delivery of L bacrylate Nanopa t al., "N ⁴ -Beheno ch, 1977, 37: 248 , et al., "Pancreat , 12: 141-146. t al., "Prodrugs of vatives," J. Med. et al., "Passage of Life Sciences, 19 ., "Pharmocokine bum, 1982, 14: l., "A Strategy fo Science, 1992, 25	ing Author, Title, Journal-Da operamide Across the Blood-Br rticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto 1-2486. ic Extracts in the Treatment of I f 9-β-D-Arabinofuranosyladenin Chem., 1978, 21(12): 1218-12. Feptides Across the Blood-Bra 196, 59 (23), 1923-1943. rtic Properties of Polyethylene (11-120. r Delivering Peptides into the C	rain Barrier 4: 325-328 sine as a Po Diabetes Me ne. 1. Synth 21. nin Barrier: Glycol Deriv	with Polysorb otential New A ellitus," The C esis and Evalu Pathophysiolo	ate 80-Coa antitumor A anadian M ation of So gical	NO X ated Agent," ed. ome 5'-
Examiner	BK & BL & BN	Alyautdin, R.N. Polybutylcyand Aoshima, M. e Cancer Researd Banting, R. G., Assoc. J. 1922 Baker, D. C. et (O-Acyl) Deriv Banks, W.A., e Perspectives," Boccu, E. et al Pharm. Res. Co. Bodor, N., et a	PUBLICATION DATE MENTS (Includ I., "Delivery of L bacrylate Nanopa t al., "N ⁴ -Beheno ch, 1977, 37: 248 , et al., "Pancreat , 12: 141-146. t al., "Prodrugs of vatives," J. Med. et al., "Passage of Life Sciences, 19 ., "Pharmocokine bum, 1982, 14: l., "A Strategy fo Science, 1992, 25	ing Author, Title, Journal-Date operamide Across the Blood-Braticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto 1-2486. ic Extracts in the Treatment of 1 f. 9-β-D-Arabinofuranosyladenia Chem., 1978, 21(12): 1218-12. Peptides Across the Blood-Bratic Properties of Polyethylene Control of Polyethylene Cont	rain Barrier 4: 325-328 sine as a Po Diabetes Me ne. 1. Synth 21. nin Barrier: Glycol Deriv	with Polysorb otential New A cellitus," The C esis and Evalu Pathophysiolo vatized Superc rous System by	ate 80-Coa ntitumor A anadian M ation of So gical oxide Dism	NO X ated agent," ed. ome 5'- utase,"
B.	BK to BL of BN verification BN verification BP of BQ &	Alyautdin, R.N. Polybutylcyand Aoshima, M. e Cancer Researd Banting, R. G., Assoc. J. 1922. Baker, D. C. et (O-Acyl) Derive Banks, W.A., e Perspectives," Boccu, E. et al Pharm. Res. Co. Bodor, N., et a Metabolism," S	PUBLICATION DATE MENTS (Includ I., "Delivery of L bacrylate Nanopa t al., "N ⁴ -Beheno ch, 1977, 37: 248 et al., "Pancreat t 12: 141-146. t al., "Prodrugs of vatives," J. Med. et al., "Passage of Life Sciences, 19 tife Sciences, 19 tife, "A Strategy fo Science, 1992, 25	ing Author, Title, Journal-Date operamide Across the Blood-Braticles," Pharm. Res. J., 1997, 1 yl-1-β-D-Arabinofuranosylcyto 1-2486. ic Extracts in the Treatment of 1 f. 9-β-D-Arabinofuranosyladenia Chem., 1978, 21(12): 1218-12. Peptides Across the Blood-Bratic Properties of Polyethylene Control of Polyethylene Cont	rain Barrier 4: 325-328 sine as a Po Diabetes Mo ne. 1. Synth 21. nin Barrier: Glycol Deriv	with Polysorb otential New A cellitus," The Cellitus," The Cellitus, and Evalue Pathophysiolo vatized Supercerous System by DATE CON Slambor	ate 80-Coantitumor Anadian Mation of Sogical oxide Dismov Sequentian SIDERED	NO X ated Agent," ded. ome 5'- utase,"

FORM PTO-1449		US Dept. of Commerce	ATTORNEY DOCKET NO.	SERIAL NO.					
		Patent and Trademark Office		09/430,735					
			4012-113 DIV2						
			APPLICANT O	A					
INFORMATION DISCLOSURE STATEMENT			Ekwuribe et al.						
(use several sheets if necessary)			DEC	19an G GROUP					
			FILING DATE	1899 (5) GROUP					
			October 29, 1999	W 1639					
	DD.	Deder N. et al. "Molecular Pa	chaging Pentide Deliver COFMA	Central Nervous System by Sequential					
U/s	BR 😉	Metabolism," Amer. Chem. Soc		pential (to) vous system by sequential					
	BS &	Brange, J. et al., "Chemical Stability of Insulin. 1. Hydrolytic Degradation During Storage of							
	5 0	Pharmaceutical Preparations," Pharm. Res., 1992, 9 (6): 715-726.							
	BT 0	Brange, J. et al., "Chemical Stat	Brange, J. et al., "Chemical Stability of Insulin. 2. Formation of Higher Molecular Weight Transformation						
	וט	Products During Storage of Pha	rmaceutical Preparations," Pharm	. Res., 1992, 9 (6): 727-734.					
	BU	Brewster, M.E., et al., "Effect o	f Molecular Manipulation on the	Estrogenic Activity of a Brain-Targeting					
	•	Estradiol Chemical Delivery Sy	stem," J. Med. Chem., 1994, 37: 4	1237-4244					
	BV			ostiturted Chemical Delivery System for					
		Estradiol Brain Targeting," J. Pharm. Sci., 1994: A-E. Brewster, M., et al., "Tissue Distribution of LY231617, an Antioxidant with Neuroprotectant Activity, in							
1/1	BW			xidant with Neuroprotectant Activity, in					
W.	DV	the Rat," J. Pharm. Studies," 1995, 84 (7): 791-793.							
	BX	Conradi, R.A., et al., "The Influence of Peptide Structure on Transport Across Caco-2 Cells," Pharm. Res., 1991, 8 (12): 1453-1459.							
4 1	BY 6	Chen, C., et al., "Extensive Biliary Excretion of the Model Opioid Peptide [D-PEN ^{2,5}] Enkephalin in Rats,"							
	D. 60	Pharm. Res. J., 14: 345-350.	muly Exerction of the Model optical replica (2 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1						
	BZ N	Chiou, G.C.Y., et al., "Systemic	G.C.Y., et al., "Systemic Delivery of Enkephalin Peptide through Eyes," Life Sciences, 1988, 43:						
		509-514.							
	CA	Chun., W., et al., "Transmucosal Delivery of Methionine Enkephalin. I: Solution Stability and Kinetics of							
<u> </u>		Degradation in Various Rabbit Mucosa Extracts," J. Pharm.Sci., 1993, 82 (4): 373-378.							
MA	CB	Fix, J.A., "Oral Controlled Release Technology for Peptides: Status and Future Prospects," Pharm. Res.,							
1111	•	1996, 13 (12): 1760-1763.							
	CC,	Gibson, A.M., et al., "Specificity of Action of Human Brain Alanyl Aminopeptidase on Leu-Enkephalin and Dynorphin-Related Peptides," Neuropeptides, 1989, 13: 259-262.							
	CD	and Dynorphin-Related Peptide	de 11 Synthesis of 5' Estare of 1	-202					
	CD 👠	Gish, D. T. et al., "Nucleic Acids. 11. Synthesis of 5'-Esters of 1-β-D-Arabinofuranosylcytosine Possessing							
 	CE	Antileukemic and Immunosuppressive Activity," J. Med. Chem., 1971, 14(12): 1159-1162. Hong, C. I. et al., "Nucleoside Conjugates. 7. Synthesis and Antitumor Activity of 1-β-D-							
	CE	Arabinofuranosyleytosine Coni	rjugates of Ether Lipids," J. Med. Chem., 1986, 29: 2038-2044.						
	CF A	Horvat, J., et al., "Synthesis and	Biological Activity of [Leu ⁵] En	kephalin Derivatives Containing D-					
		Horvat, J., et al., "Synthesis and Biological Activity of [Leu ⁵] Enkephalin Derivatives Containing D-Glucose," J. Peptide Protein Res., 1988, 31: 499-507.							
CG N		Hostetler, K. Y. et al., "Synthesis and Antiretroviral Activity of Phospholipid Analogs of Azidothymidine							
 	v	and Other Antiviral Nucleosides," The Journal of Biological Chemistry, 1990, 265(11): 6112-6117.							
СНо		Kroll, R.A., et al., "Outwitting the Blood-Brain Barrier for Therapeutic Purposes: Osmotic Opening and							
		Other Means," 1998 Neurosurg	gery, 42 (5): 1083-1100.						
	CI 🔞	Maislos, M. et al., "The Source of the Circulating Aggregate of Insulin in Type I Diabetic Patients							
	-	Therapeutic Insulin," J. Clin. Ir	ivest., 1986, 77: 717-723.	1 CM - 4.1 P. 1 - 1 - 11 . 11					
	Cl 🚱	Mosnaim, A.D., et al., "Studies		egradation of Methionine-Enkephalin,"					
	1 1/2	Gen. Pharmac., 1988, 19 (5): 729-733. Nestor, J., "Improved Duration of Action of Peptide Drugs," Amer. Chem Soc. 1995: 449-471.							
	CK vo								
120	CLm Oka, K. et al., "Enhanced Intestinal Absorption of a Hydrophobic Polymer-Conjugated Protein Drug,								
111		Smancs, in an Oily Formulation	n," Pharm. Res., 1990, 7 (8): 852-	-855.					
"			Continue on Page 4						
Examiner				DATE CONSIDERED					
	B	CCISA		4/2,103					
EXAMINER	: Initia	if citation considered, whether of	or not citation is in conformance we	rith MPEP § 609; Draw line through					

		هد. ه	<i>y</i> ,			•		Sheet 12 0
FORM PTO		U.S. Department nt and Trademark		Ĭ	Attorney Do	cket Number 9233-8DV2		Serial No. 09/430,735
LIST	OF DO	CUMENTS CITI	D BY APPLI	CANT				
OIP								
0	~\\	se several sheets if	necessary)		A			
NOV 0 6 200	r (2)				Applicants:	Ekwu	ribe et al.	
PADEMARY	Griss			0.1.00.1000			Group	
CADEMI.			U. S	S. PATENT DO	CUMENTS			1021
Examiner Initial		Document Number	Date		ame	Class	Subclass	Filing Date if Appropriate
UL	1.	5,681,811	10/28/97	Ekwuribe		514	8	
1/1/	2.	5,693,769	12/02/97	Kahne et al.		536	5	·——
			- ·					
		 						
		 		 	PEO			
					REC. NOV.	E/12		
		<u> </u>		1	CHO O	E	y	
	<u> </u>				TEN .	2002		
						V/20-		
			<u> </u>			1480g		
			L	<u> </u>		<u> </u>		
	T	·	FORE	IGN PATENT I	OCUMENTS	r	7	
		Document Number	Date	Co	untry	Class	Subclass	Translation Yes No
	•							
	*	OTHER DO	CUMENTS (I	ncluding Author	, Title, Date, Pe	rtinent Pages	, Etc.)	
				<u> </u>			·	
					· · · · · · · · · · · · · · · · · · ·		·	
			<u> </u>					
	1	1						ll l

EXAMINER EXAMINER

B. ceisa

DATE CONSIDERED

5/21/03